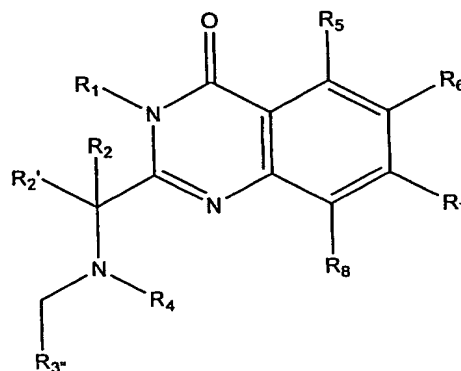
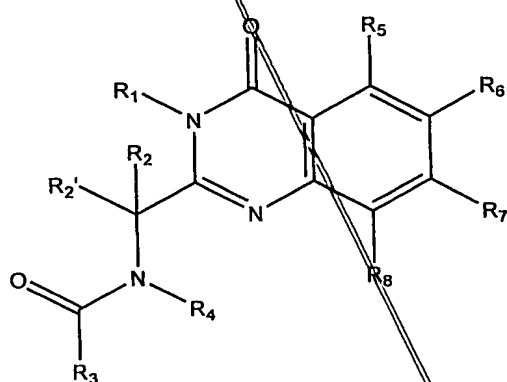
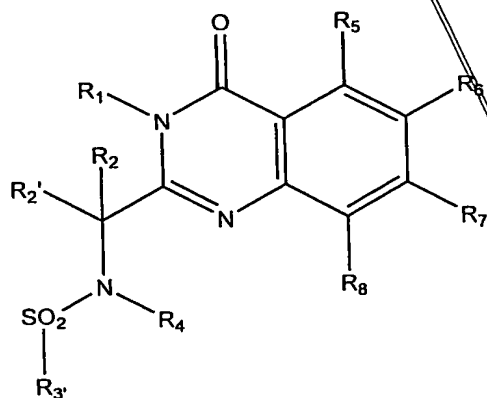


We claim:

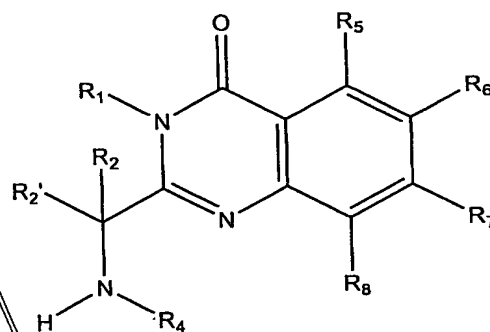
1. A method of treating cellular proliferative diseases comprising administering a compound chosen from the group consisting of:



5



and



wherein:

- $R_1$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;
- 10  $R_2$  and  $R_2'$  are independently chosen from hydrogen, alkyl, oxaalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl; or  $R_2$  and  $R_2'$  taken together form a 3- to 7-membered ring;
- 15  $R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, oxaalkyl, oxaalkylaryl, substituted oxaalkylaryl,  $R_{15}O-$  and  $R_{15}-NH-$ ;

$R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, and  $R_{15}$ -NH-;

5  $R_{3''}$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

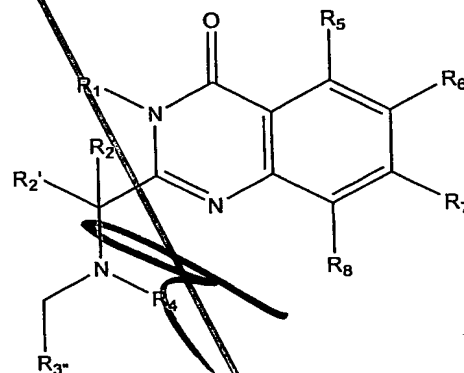
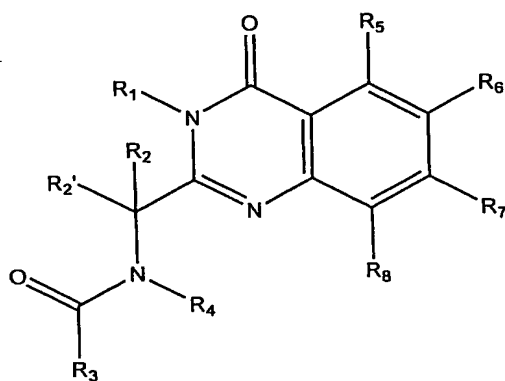
$R_4$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, and  $R_{16}$ -alkylene-;

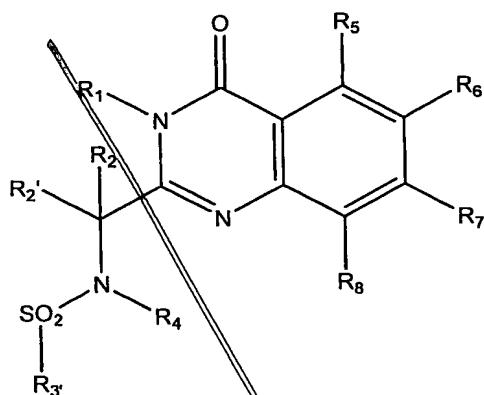
10  $R_5, R_6, R_7$  and  $R_8$  are independently chosen from hydrogen, alkyl, alkoxy, halogen, fluoroalkyl, nitro, dialkylamino, alkylsulfonyl, alkylsulfonamido, sulfonamidoalkyl, sulfonamidoaryl, alkylthio, carboxyalkyl, carboxamido, aminocarbonyl, aryl and heteroaryl;

15  $R_{15}$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

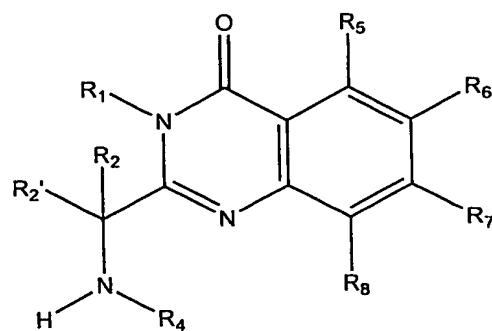
$R_{16}$  is chosen from alkoxy, amino, alkylamino, dialkylamino, N-heterocyclyl and substituted N-heterocyclyl.

2. A method of treating a disorder associated with KSP kinesin activity comprising administering a compound chosen from the group consisting of:





and



wherein:

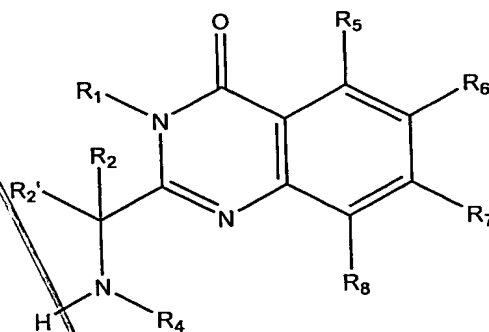
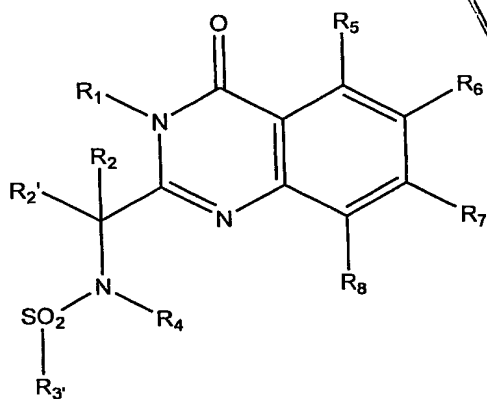
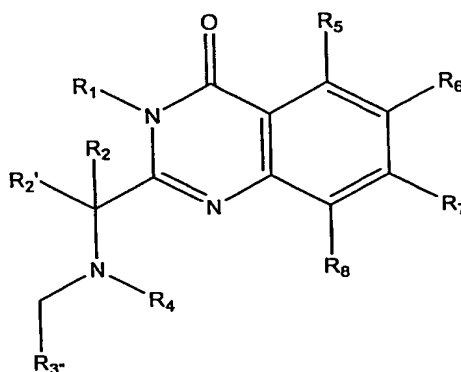
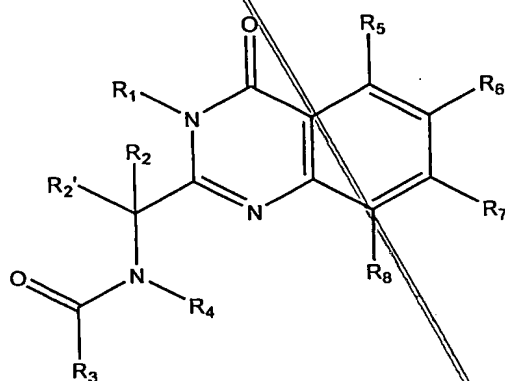
- $R_1$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;
- $R_2$  and  $R_2'$  are independently chosen from hydrogen, alkyl, oxaalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl; or  $R_2$  and  $R_2'$  taken together form a 3- to 7-membered ring;
- $R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, oxaalkyl, oxaalkylaryl, substituted oxaalkylaryl,  $R_{15}O$ - and  $R_{15}NH$ -;
- $R_3'$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl and  $R_{15}NH$ -;
- $R_{3''}$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;
- $R_4$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, and  $R_{16}$ -alkylene-;
- $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are independently chosen from hydrogen, alkyl, alkoxy, halogen, fluoroalkyl, nitro, dialkylamino, alkylsulfonyl, alkylsulfonamido, sulfonamidoalkyl, sulfonamidoaryl, alkylthio, carboxyalkyl, carboxamido,

aminocarbonyl, aryl and heteroaryl;

$R_{13}$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

- 5  $R_{16}$  is chosen from alkoxy, amino, alkylamino, dialkylamino, N-heterocyclyl and substituted N-heterocyclyl.

3. A method of inhibiting KSP kinesin comprising contacting KSP kinesin with a compound chosen from the group consisting of:



and

wherein:

$R_1$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

15

$R_2$  and  $R_2'$  are independently chosen from hydrogen, alkyl, oxaalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl; or  $R_2$  and  $R_2'$  taken together form a 3- to 7-membered ring;

- $R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, oxaalkyl, oxaalkylaryl, substituted oxaalkylaryl,  $R_{15}$ -O- and  $R_{15}$ -NH-;
- 5  $R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl and  $R_{15}$ -NH-;
- $R_{3..}$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;
- 10  $R_4$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, and  $R_{16}$ -alkylene-;
- $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are independently chosen from hydrogen, alkyl, alkoxy, halogen, fluoroalkyl, nitro, dialkylamino, alkylsulfonyl, alkylsulfonamido, sulfonamidoalkyl, sulfonamidoaryl, alkylthio, carboxyalkyl, carboxamido, aminocarbonyl, aryl and heteroaryl;
- 15  $R_{15}$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;
- 20  $R_{16}$  is chosen from alkoxy, amino, alkylamino, dialkylamino, N-heterocyclyl and substituted N-heterocyclyl.

4. A method according to claim 1, 2 or 3 wherein

R<sub>1</sub> is chosen from hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, heteroaryl, substituted heteroaryl, alkylaryl, substituted alkylaryl and substituted alkylheteroaryl;

5 R<sub>2</sub> is chosen from hydrogen, alkyl and substituted alkyl;

R<sub>2</sub>' is hydrogen;

R<sub>3</sub> is chosen from alkyl, substituted alkyl, alkylaryl, heteroaryl, aryl, substituted aryl, substituted heteroaryl, substituted oxaalkylaryl R<sub>15</sub>O- and R<sub>15</sub>-NH-;

10 R<sub>4</sub> is chosen from alkyl, aryl, alkylaryl, alkylheteroaryl, substituted alkyl, substituted aryl, and R<sub>16</sub>-alkylene-;

R<sub>5</sub> is hydrogen;

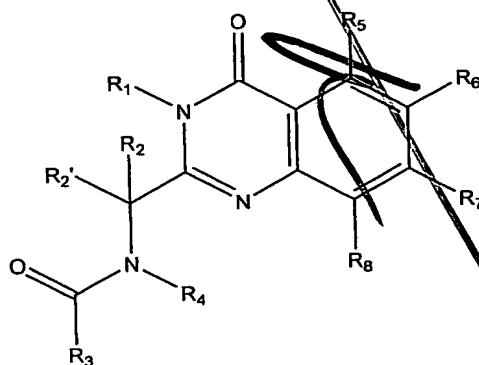
R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently chosen from hydrogen, halogen, methyl and trifluoromethyl;

R<sub>15</sub> is chosen from alkyl, aryl and substituted aryl;

15 R<sub>16</sub> is chosen from alkoxy, amino, alkylamino, dialkylamino and N-heterocycl.

5. A method according to claim 4 wherein the stereogenic center to which R<sub>2</sub> and R<sub>2</sub>' are attached is of the R configuration.

20 6. A method according to claim 1, 2 or 3 comprising administering a compound of formula:



7. A method according to claim 6 wherein R<sub>1</sub> is chosen from hydrogen, lower alkyl, substituted lower alkyl, benzyl, substituted benzyl, phenyl, naphthyl and substituted phenyl.

8. A method according to claim 7 wherein R<sub>1</sub> is chosen from hydrogen, ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, tetrahydrofuranylmethyl and (ethoxycarbonyl)ethyl.

9. A method according to claim 6 wherein R<sub>2</sub> is chosen from hydrogen, lower alkyl and substituted lower alkyl, and R<sub>2</sub>' is hydrogen.

10. A method according to claim 9 wherein R<sub>2</sub> is chosen from hydrogen, methyl, ethyl, propyl, methylthioethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, hydroxymethyl, benzyl and indolylmethyl.

11. A method according to claim 6 wherein R<sub>3</sub> is chosen from C<sub>1</sub>-C<sub>13</sub> alkyl; substituted lower alkyl; phenyl; naphthyl; phenyl substituted with one or more halo, lower alkyl, loweralkoxy, nitro, carboxy, methylenedioxy or trifluoromethyl; biphenyl; benzyl; phenoxymethyl; halophenoxymethyl; phenylvinyl; heteroaryl; heteroaryl substituted with lower alkyl; and benzyloxymethyl.

12. A method according to claim 11 wherein R<sub>3</sub> is chosen from ethyl, propyl, chloropropyl, butoxy, heptyl, butyl, octyl, tridecanyl, (ethoxycarbonyl)ethyl, dimethylaminoethyl, dimethylaminomethyl, phenyl, naphthyl, halophenyl, dihalophenyl, cyanophenyl, halo(trifluoromethyl)phenyl, chlorophenoxymethyl, methoxyphenyl, carboxyphenyl, ethylphenyl, tolyl, biphenyl, methylenedioxyphenyl, methylsulfonylphenyl, methoxychlorophenyl, chloronaphthyl, methylhalophenyl, trifluoromethylphenyl, butylphenyl, pentylphenyl, methylnitrophenyl, phenoxymethyl, dimethoxyphenyl, phenylvinyl, nitrochlorophenyl, nitrophenyl, dinitrophenyl, bis(trifluoromethyl)phenyl,

benzyloxymethyl, benzyl, furanyl, benzofuranyl, pyridinyl, indolyl, methylpyridinyl, quinolinyl, picolinyl, pyrazolyl, and imidazolyl.

13. A method according to claim 6 wherein  $R_3$  is  $R_{15}$ -NH- and  $R_{15}$  is chosen from lower alkyl; cyclohexyl; phenyl; and phenyl substituted with halo, lower alkyl, loweralkoxy, or lower alkylthio.

14. A method according to claim 13 wherein  $R_{15}$  is chosen from isopropyl, butyl, cyclohexyl, phenyl, bromophenyl, dichlorophenyl, methoxyphenyl, ethylphenyl, tolyl, trifluoromethylphenyl and methylthiophenyl.

15. A method according to claim 6 wherein  $R_4$  is chosen from lower alkyl, substituted lower alkyl, cyclohexyl; phenyl substituted with hydroxy, lower alkoxy or lower alkyl; benzyl; heteroarylmethyl; heteroarylethyl; heteroarylpropyl and  $R_{16}$ -alkylene-, wherein  $R_{16}$  is amino, lower alkylamino, di(lower alkyl)amino, lower alkoxy, or N-heterocyclyl.

16. A method according to claim 15 wherein  $R_4$  is chosen from methyl, ethyl, propyl, butyl, cyclohexyl, carboxyethyl, carboxymethyl, methoxyethyl, hydroxyethyl, hydroxypropyl, dimethylaminoethyl, dimethylaminopropyl, diethylaminoethyl, diethylaminopropyl, aminopropyl, methylaminopropyl, 2,2-dimethyl-3-(dimethylamino)propyl, 1-cyclohexyl-4-(diethylamino)butyl, aminoethyl, aminobutyl, aminopentyl, aminoethyl, aminoethoxyethyl, isopropylaminopropyl, diisopropylaminoethyl, 1-methyl-4-(diethylamino)butyl, (t-Boc)aminopropyl, hydroxyphenyl, benzyl, methoxyphenyl, methylmethoxyphenyl, dimethylphenyl, tolyl, ethylphenyl, (oxopyrrolidinyl)propyl, (methoxycarbonyl)ethyl, benzylpiperidinyl, pyridinylethyl, pyridinylmethyl, morpholinylethyl, morpholinylpropyl, piperidinyl, azetidinylmethyl, azetidinypropyl, pyrrolidinylethyl, pyrrolidinylpropyl, piperidinylmethyl, piperidinylethyl, imidazolylpropyl, imidazolylethyl, (ethylpyrrolidinyl)methyl, (methylpyrrolidinyl)ethyl, (methylpiperidinyl)propyl, (methylpiperazinyl)propyl, furanylmethyl and indolylethyl.



17. A method according to claim 6 wherein

- $R_1$  is chosen from lower alkyl, benzyl, substituted benzyl and substituted phenyl;
- $R_2$  is chosen from hydrogen, alkyl, substituted lower alkyl and benzyl;
- $R_2'$  is hydrogen;
- 5  $R_3$  is chosen from substituted phenyl and naphthyl;
- $R_4$  is chosen from substituted alkyl and  $R_{16}$ -alkylene-;
- $R_5$  is hydrogen or halo
- $R_6$  is hydrogen, methyl or halo;
- $R_7$  is hydrogen, halo, methyl or trifluoromethyl;
- 10  $R_8$  is hydrogen or halo;
- $R_{16}$  is chosen from di(lower alkylamino), (lower alkyl)amino, amino, N-heterocyclyl and substituted N-heterocyclyl.

18. A method according to claim 1, 2 or 3 wherein

- 15  $R_1$  is benzyl or halobenzyl;
- $R_2$  is chosen from ethyl and propyl;
- $R_2'$  is hydrogen;
- $R_3$  is substituted phenyl;
- $R_3'$  is substituted phenyl;
- 20  $R_{3''}$  is substituted phenyl;
- $R_4$  is  $(CH_2)_m OH$  or  $(CH_2)_p R_{16}$  wherein  $m$  is 2 or 3 and  $p$  is 1-3;
- $R_5$  is hydrogen;
- $R_6$  is hydrogen;
- $R_7$  is halo;
- 25  $R_8$  is hydrogen;
- $R_{16}$  is chosen from amino, propylamino, and azetidiny.

19. A method according to claim 18 wherein the stereogenic center to which  $R_2$  and  $R_2'$  are attached is of the R configuration.

30

20. A method according to claim 1, 2 or 3 comprising administering a compound of formula:

$R_1$  is chosen from hydrogen, lower alkyl, substituted lower alkyl, benzyl, substituted benzyl, phenyl, naphthyl and substituted phenyl;

R<sub>3</sub> is chosen from C<sub>1</sub>-C<sub>13</sub> alkyl; phenyl; naphthyl; phenyl substituted with halo, lower alkyl, lower alkoxy, nitro, methylenedioxy, or trifluoromethyl; biphenyl, benzyl and heteroaryl; and

R<sub>16</sub> is amino, (lower alkyl)amino, di(lower alkyl)amino, lower alkoxy, or N-heterocyclyl.

R<sub>1</sub> is chosen from lower alkyl, benzyl, substituted benzyl and substituted phenyl;

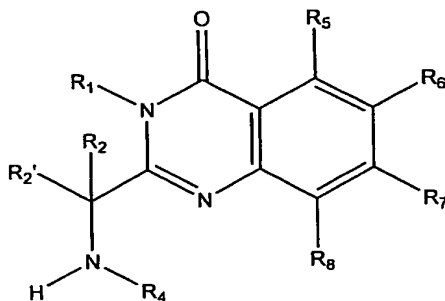
$R_2'$  is hydrogen;

20 R<sub>4</sub> is R<sub>16</sub>-alkylene- hydroxy lower alkyl or carboxy lower alkyl;

R<sub>5</sub> and R<sub>8</sub> are hydrogen;

R<sub>16</sub> is chosen from di(lower alkylamino), (lower alkyl)amino, amino, piperidinyl, azetidiny, pyrrolidinyl and morpholinyl.

23. A method according to claim 1, 2 or 3 comprising administering a compound of formula:



24. A method according to claim 23 wherein:

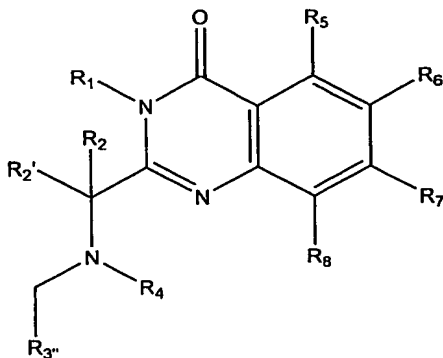
- 5 R<sub>1</sub> is chosen from hydrogen, lower alkyl, substituted lower alkyl, benzyl, substituted benzyl, phenyl, naphthyl and substituted phenyl;  
R<sub>2</sub> is chosen from hydrogen, lower alkyl and substituted lower alkyl and R<sub>2</sub>' is hydrogen; and  
R<sub>4</sub> is chosen from lower alkyl, cyclohexyl; phenyl substituted with hydroxy, lower alkoxy or lower alkyl; benzyl; heteroarylmethyl; heteroarylethyl;  
10 heteroarylpropyl and R<sub>16</sub>-alkylene, wherein R<sub>16</sub> is di(lower alkyl)amino, alkylamino, amino, lower alkoxy, or N-heterocyclyl.

25. A method according to claim 23 wherein

- R<sub>1</sub> is chosen from lower alkyl, benzyl, substituted benzyl and substituted phenyl;  
15 R<sub>2</sub> is hydrogen or lower alkyl;  
R<sub>2</sub>' is hydrogen;  
R<sub>4</sub> is R<sub>16</sub>-alkylene-;  
R<sub>6</sub> and R<sub>7</sub> are chosen from hydrogen and halo;  
R<sub>5</sub> and R<sub>8</sub> are hydrogen;  
20 R<sub>16</sub> is chosen from di(lower alkylamino), (lower alkyl)amino, amino, pyrrolidinyl, piperidinyl, imidazolyl and morpholinyl.

26. A method according to claim 1, 2 or 3 comprising administering a

compound of formula:



27. A method according to claim 26 wherein:

R<sub>1</sub> is chosen from hydrogen, lower alkyl, substituted lower alkyl, benzyl, substituted  
5 benzyl, phenyl, naphthyl and substituted phenyl;

R<sub>2</sub> is chosen from hydrogen, lower alkyl and substituted lower alkyl and R<sub>2</sub>' is  
hydrogen;

R<sub>3</sub> is chosen from C<sub>1</sub>-C<sub>13</sub> alkyl; substituted lower alkyl; phenyl; naphthyl; phenyl  
10 substituted with halo, lower alkyl, lower alkoxy, nitro, methylenedioxy, or  
trifluoromethyl; biphenyl; benzyl and heterocyclyl; and

R<sub>4</sub> is chosen from lower alkyl, substituted lower alkyl; cyclohexyl; phenyl substituted  
with hydroxy, lower alkoxy or lower alkyl; benzyl; substituted benzyl;  
heterocyclyl; heteroarylmethyl; heteroarylethyl; heteroarylpropyl and R<sub>16</sub>-  
alkylene, wherein

15 R<sub>16</sub> is di(lower alkyl)amino, (lower alkyl)amino, amino, lower alkoxy, or N-  
heterocyclyl.

28. A method according to claim 27 wherein

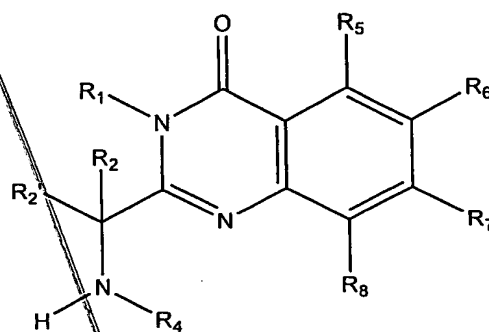
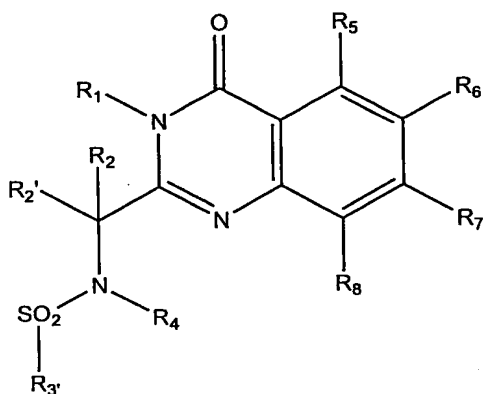
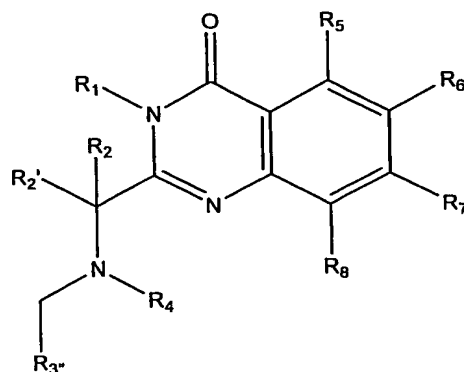
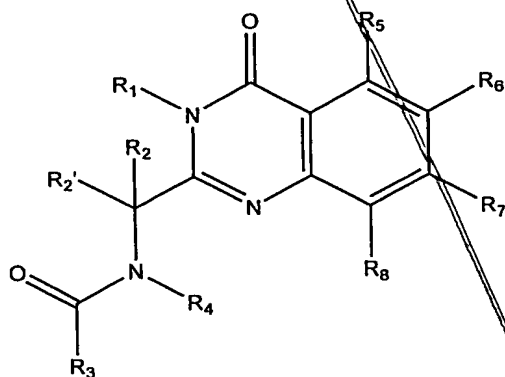
- $R_1$  is chosen from lower alkyl, benzyl, substituted benzyl and substituted phenyl;  
 $R_2$  is hydrogen or lower alkyl;  
 $R_2'$  is hydrogen;  
 5  $R_{3..}$  is chosen from substituted phenyl, heterocyclyl and naphthyl;  
 $R_4$  is chosen from substituted benzyl, heterocyclyl substituted lower alkyl and  $R_{16}$ -alkylene-;  
 $R_6$  and  $R_7$  are chosen from hydrogen and halo;  
 $R_5$  and  $R_8$  are hydrogen;  
 10  $R_{16}$  is chosen from di(lower alkylamino), (lower alkyl)amino, amino, pyrrolidinyl, azetidiny piperidinyl, imidazolyl and morpholinyl.

29. A method according to claim 28 wherein

- $R_1$  is benzyl;  
 $R_2$  is ethyl;  
 15  $R_2'$  is hydrogen;  
 $R_{3..}$  is chosen from halophenyl, polyhalophenyl, tolyl, dimethylphenyl, methoxyphenyl, dimethoxyphenyl, cyanophenyl, trifluoromethylphenyl, trifluoromethoxyphenyl, bis(trifluoromethyl)phenyl, carboxyphenyl, t-butylphenyl, methoxycarbonylphenyl, piperidinyl and naphthyl;  
 20  $R_4$  is chosen from substituted benzyl, piperidinyl, hydroxy (lower alkyl) and  $R_{16}$ -alkylene-;  
 $R_6$  and  $R_7$  are chosen from hydrogen and halo;  
 $R_5$  and  $R_8$  are hydrogen;  
 $R_{16}$  is chosen from dimethylamino, amino, pyrrolidinyl and piperidinyl.

- 25 30. A method according to claim 1 or 2 wherein said disease or disorder is chosen from the group consisting of cancer, hyperplasia, restenosis, cardiac hypertrophy, immune disorders and inflammation.

31. A compound chosen from the group consisting of:



and

5

wherein:

$R_1$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

10  $R_2$  and  $R_2'$  are independently chosen from hydrogen, alkyl, oxaalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl; or  $R_2$  and  $R_2'$  taken together form a 3- to 7-membered ring;

15  $R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, oxaalkyl, oxaalkylaryl, substituted oxaalkylaryl,  $R_{15}O-$  and  $R_{15}NH-$ ;

*B2*  
*cont*  
5  $R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl and  $R_{15}$ -NH-;

$R_{3'}$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

$R_4$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, and  $R_{16}$ -alkylene-;

10  $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are independently chosen from hydrogen, alkyl, alkoxy, halogen, fluoroalkyl, nitro, dialkylamino, alkylsulfonyl, alkylsulfonamido, sulfonamidoalkyl, sulfonamidoaryl, alkylthio, carboxyalkyl, carboxamido, aminocarbonyl, aryl and heteroaryl;

15  $R_{15}$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

$R_{16}$  is chosen from alkoxy, amino, alkylamino, dialkylamino, N-heterocyclyl and substituted N-heterocyclyl;

20 with the proviso that when  $R_3$  is  $R_{15}$ -NH- attached to carbonyl, both of  $R_2$  and  $R_4$  must be other than hydrogen.

32. A compound according to claim 31 wherein

$R_1$  is chosen from hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, heteroaryl, substituted heteroaryl, alkylaryl, alkylheteroaryl and substituted alkylaryl;

$R_2$  is chosen from hydrogen, alkyl and substituted alkyl;

25  $R_2'$  is hydrogen;

$R_3$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, substituted aryl, substituted alkyl, substituted heteroaryl, oxaalkylaryl, substituted oxaalkylaryl,  $R_{15}$ O- and  $R_{15}$ -NH-;

30  $R_4$  is chosen from alkyl, aryl, alkylaryl, alkylheteroaryl, substituted alkyl, substituted aryl, and  $R_{16}$ -alkylene-;

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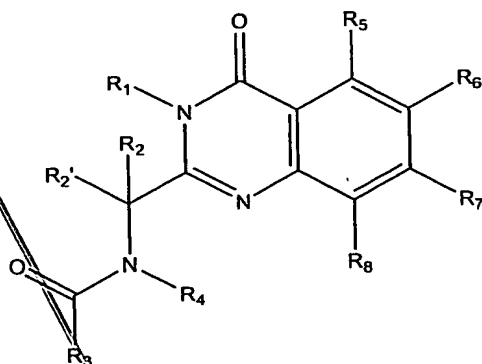
~~R<sub>5</sub> is hydrogen;~~

~~R<sub>6</sub>, R<sub>7</sub> and R<sub>8</sub> are independently chosen from hydrogen, halogen, methyl and trifluoromethyl;~~

~~R<sub>15</sub> is chosen from alkyl, aryl and substituted aryl;~~

5 ~~R<sub>16</sub> is chosen from alkoxy, amino, alkylamino, dialkylamino and N-heterocyclyl.~~

33. A compound according to claim 31 of formula:



34. A compound according to claim 33 wherein R<sub>1</sub> is chosen from hydrogen, lower alkyl, substituted lower alkyl, benzyl, substituted benzyl, phenyl, naphthyl and substituted phenyl.

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35. A compound according to claim 34 wherein R<sub>1</sub> is chosen from hydrogen, ethyl, propyl, methoxyethyl, naphthyl, phenyl, bromophenyl, chlorophenyl, methoxyphenyl, ethoxyphenyl, tolyl, dimethylphenyl, chlorofluorophenyl, methylchlorophenyl, ethylphenyl, phenethyl, benzyl, chlorobenzyl, methylbenzyl, methoxybenzyl, tetrahydrofuranylmethyl and (ethoxycarbonyl)ethyl.

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36. A compound according to claim 33 wherein R<sub>2</sub> is chosen from hydrogen, lower alkyl and substituted lower alkyl, and R<sub>2</sub>' is hydrogen.

37. A compound according to claim 36 wherein R<sub>2</sub> is chosen from hydrogen, methyl, ethyl, propyl, methylthioethyl, aminobutyl, (CBZ)aminobutyl, cyclohexylmethyl, benzyloxymethyl, methylsulfinylethyl, methylsulfinylmethyl, hydroxymethyl, benzyl and indolylmethyl.

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38. A compound according to claim 33 wherein  $R_3$  is chosen from  $C_1$ - $C_{13}$  alkyl; substituted lower alkyl; phenyl; naphthyl; phenyl substituted with one or more halo, lower alkyl, loweralkoxy, nitro, carboxy, methylenedioxy, or trifluoromethyl; biphenyl; benzyl; phenoxymethyl; halophenoxymethyl; phenylvinyl; heteroaryl; heteroaryl substituted with lower alkyl; and benzyloxymethyl.

39. A compound according to claim 38 wherein  $R_3$  is chosen from ethyl, propyl, chloropropyl, butoxy, heptyl, butyl, octyl, tridecanyl, (ethoxycarbonyl)ethyl, dimethylaminoethyl, dimethylaminomethyl, phenyl, naphthyl, halophenyl, dihalophenyl, cyanophenyl, halo(trifluoromethyl)phenyl, chlorophenoxymethyl, methoxyphenyl, carboxyphenyl, ethylphenyl, tolyl, biphenyl, methylenedioxyphenyl, methylsulfonylphenyl, methoxychlorophenyl, chloronaphthyl, methylhalophenyl, trifluoromethylphenyl, butylphenyl, pentylphenyl, methylnitrophenyl, phenoxymethyl, dimethoxyphenyl, phenylvinyl, nitrochlorophenyl, nitrophenyl, dinitrophenyl, bis(trifluoromethyl)phenyl, benzyloxymethyl, benzyl, furanyl, benzofuranyl, pyridinyl, indolyl, methylpyridinyl, quinolinyl, picolinyl, pyrazolyl, and imidazolyl.

40. A compound according to claim 33 wherein  $R_3$  is  $R_{15}$ -NH- and  $R_{15}$  is chosen from lower alkyl; cyclohexyl; phenyl; and phenyl substituted with halo, lower alkyl, loweralkoxy, or lower alkylthio.

41. A compound according to claim 40 wherein  $R_{15}$  is chosen from isopropyl, butyl, cyclohexyl, phenyl, bromophenyl, dichlorophenyl, methoxyphenyl, ethylphenyl, tolyl, trifluoromethylphenyl and methylthiophenyl.

42. A compound according to claim 33 wherein  $R_4$  is chosen from lower alkyl, substituted lower alkyl, cyclohexyl; phenyl substituted with hydroxy, lower alkoxy or lower alkyl; benzyl; heteroarylmethyl; heteroarylethyl; heteroarylpropyl and  $R_{16}$ -alkylene-, wherein  $R_{16}$  is amino, lower alkylamino, di(lower alkyl)amino, lower alkoxy, or N-heterocyclyl.

43. A compound according to claim 42 wherein  $R_4$  is chosen from methyl, ethyl, propyl, butyl, cyclohexyl, carboxyethyl, carboxymethyl, methoxyethyl, hydroxyethyl, hydroxypropyl, dimethylaminoethyl, dimethylaminopropyl, diethylaminoethyl, diethylaminopropyl, aminopropyl, methylaminopropyl, , 2,2-dimethyl-3-(dimethylamino)propyl, 1-cyclohexyl-4-(diethylamino)butyl, aminoethyl, aminobutyl, aminopentyl, aminoethyl, aminoethoxyethyl, isopropylaminopropyl, diisopropylaminoethyl, 1-methyl-4-(diethylamino)butyl, (t-Boc)aminopropyl, hydroxyphenyl, benzyl, methoxyphenyl, methylmethoxyphenyl, dimethylphenyl, tolyl, ethylphenyl, (oxopyrrolidinyl)propyl, (methoxycarbonyl)ethyl, benzylpiperidinyl, pyridinylethyl, pyridinylmethyl, morpholinylethyl, morpholinylpropyl, piperidinyl, azetidinylmethyl, azetidylpropyl pyrrolidinylethyl, pyrrolidinylpropyl, piperidinylmethyl, piperidinylethyl, imidazolylpropyl, imidazolylethyl, (ethylpyrrolidinyl)methyl, (methylpyrrolidinyl)ethyl, (methylpiperidinyl)propyl, (methylpiperazinyl)propyl, furanylmethyl and indolylethyl.

44. A compound according to claim 33 wherein  $R_1$  is chosen from lower alkyl, benzyl, substituted benzyl and substituted phenyl;  $R_2$  is chosen from hydrogen, alkyl, substituted lower alkyl and benzyl;  $R_2'$  is hydrogen;  $R_3$  is chosen from substituted phenyl and naphthyl;  $R_4$  is chosen from substituted alkyl and  $R_{16}$ -alkylene-;  $R_5$  is hydrogen or halo;  $R_6$  is hydrogen, methyl or halo;  $R_7$  is hydrogen, halo, methyl or trifluoromethyl;  $R_8$  is hydrogen or halo;  $R_{16}$  is chosen from di(lower alkylamino), (lower alkyl)amino, amino N-heterocyclyl and substituted N-heterocyclyl.

45. A compound according to claim 31 wherein  $R_1$  is benzyl or halobenzyl;  $R_2$  is chosen from ethyl and propyl;  $R_2'$  is hydrogen;

R<sub>3</sub> is substituted phenyl;

R<sub>3'</sub> is substituted phenyl;

R<sub>3''</sub> is substituted phenyl;

R<sub>4</sub> is (CH<sub>2</sub>)<sub>m</sub> OH or (CH<sub>2</sub>)<sub>p</sub> R<sub>16</sub> wherein m is 2 or 3 and p is 1-3;

5 R<sub>5</sub> is hydrogen;

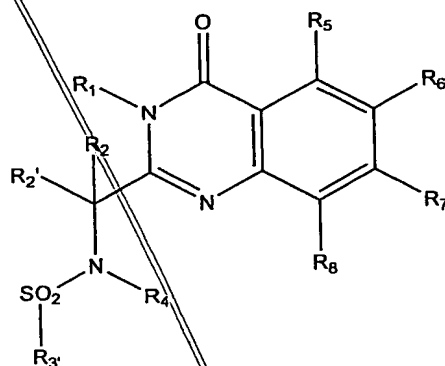
R<sub>6</sub> is hydrogen;

R<sub>7</sub> is halo;

R<sub>8</sub> is hydrogen;

R<sub>16</sub> is chosen from amino, propylamino, and azetidiny.

10 46. A compound according to claim 31 of formula:



47. A compound according to claim 46 wherein:

R<sub>1</sub> is chosen from hydrogen, lower alkyl, substituted lower alkyl, benzyl, substituted benzyl, phenyl, naphthyl and substituted phenyl;

15 R<sub>2</sub> is chosen from hydrogen, lower alkyl and substituted lower alkyl and R<sub>2'</sub> is hydrogen;

R<sub>3'</sub> is chosen from C<sub>1</sub>-C<sub>13</sub> alkyl; phenyl; naphthyl; phenyl substituted with halo, lower alkyl, lower alkoxy, nitro, methylenedioxy, or trifluoromethyl; biphenyl, benzyl and heteroaryl; and

20 R<sub>4</sub> is chosen from lower alkyl, substituted lower alkyl, cyclohexyl; phenyl substituted with hydroxy, lower alkoxy or lower alkyl; benzyl; heteroarylmethyl; heteroarylethyl; heteroarylpropyl and R<sub>16</sub>-alkylene, wherein

R<sub>16</sub> is amino, (lower alkyl)amino, di(lower alkyl)amino, lower alkoxy, or N-heterocyclyl.

48. A compound according to claim 47 wherein

R<sub>1</sub> is chosen from lower alkyl, benzyl, substituted benzyl and substituted phenyl;

R<sub>2</sub> is hydrogen or lower alkyl;

R<sub>2</sub>' is hydrogen;

5 R<sub>3</sub> is chosen from substituted phenyl and naphthyl;

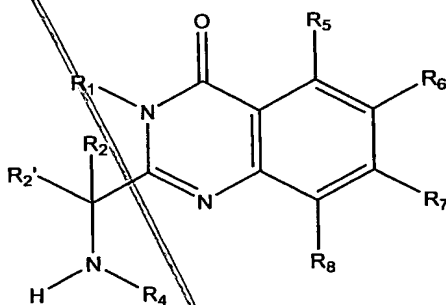
R<sub>4</sub> is R<sub>16</sub>-alkylene-, hydroxy(lower alkyl) or carboxy (lower alkyl);

R<sub>7</sub> is hydrogen, fluoro, chloro or methyl;

R<sub>5</sub>, R<sub>6</sub> and R<sub>8</sub> are hydrogen;

10 R<sub>16</sub> is chosen from di(lower alkyl)amino, (lower alkyl)amino, amino, pyrrolidinyl and piperidinyl.

49. A compound according to claim 31 of formula:



50. A compound according to claim 49 wherein:

15 R<sub>1</sub> is chosen from hydrogen, lower alkyl, substituted lower alkyl, benzyl, substituted benzyl, phenyl, naphthyl and substituted phenyl;

R<sub>2</sub> is chosen from hydrogen, lower alkyl and substituted lower alkyl and R<sub>2</sub>' is hydrogen; and

20 R<sub>4</sub> is chosen from lower alkyl, cyclohexyl; phenyl substituted with hydroxy, lower alkoxy or lower alkyl; benzyl; heteroarylmethyl; heteroarylethyl; heteroarylpropyl and R<sub>16</sub>-alkylene, wherein R<sub>16</sub> is di(lower alkyl)amino, (lower alkyl)amino, amino, lower alkoxy, or N-heterocyclyl.

51. A compound according to claim 49 wherein

$R_1$  is chosen from lower alkyl, benzyl, substituted benzyl and substituted phenyl;

$R_2$  is hydrogen or lower alkyl;

$R_2'$  is hydrogen;

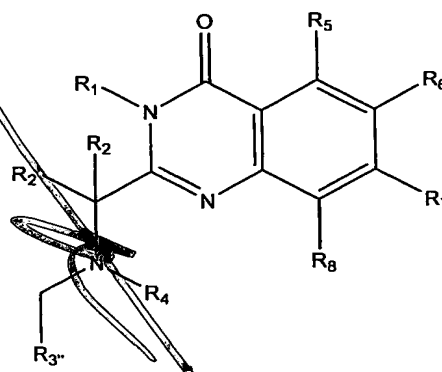
$R_4$  is  $R_{16}$ -alkylene-;

5  $R_7$  is hydrogen, fluoro, chloro or methyl;

$R_5$ ,  $R_6$  and  $R_8$  are hydrogen;

$R_{16}$  is chosen from di(lower alkylamino), (lower alkyl)amino, amino, pyrrolidinyl, piperidinyl, imidazolyl and morpholinyl.

52. A compound according to claim 31 of formula:



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53. A compound according to claim 52 wherein:

$R_1$  is chosen from hydrogen, lower alkyl, substituted lower alkyl, benzyl, substituted benzyl, phenyl, naphthyl and substituted phenyl;

$R_2$  is chosen from hydrogen, lower alkyl and substituted lower alkyl and  $R_2'$  is hydrogen;

15

$R_3$  is chosen from  $C_1$ - $C_{13}$  alkyl; substituted lower alkyl; phenyl; naphthyl; phenyl substituted with halo, lower alkyl, lower alkoxy, nitro, methylenedioxy, or trifluoromethyl; biphenyl, benzyl and heterocyclyl; and

$R_4$  is chosen from lower alkyl, substituted lower alkyl, cyclohexyl; phenyl substituted with hydroxy, lower alkoxy or lower alkyl; benzyl; substituted benzyl, heterocyclyl, heteroarylmethyl; heteroarylethyl; heteroarylpropyl and  $R_{16}$ -alkylene, wherein

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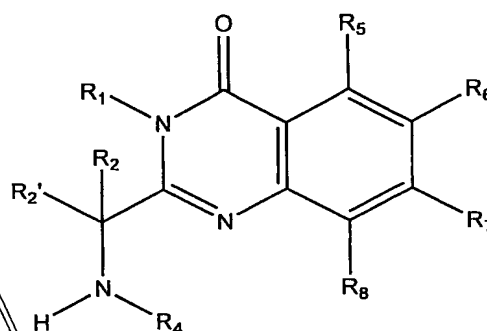
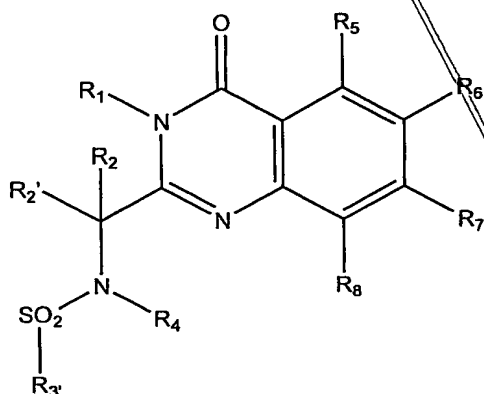
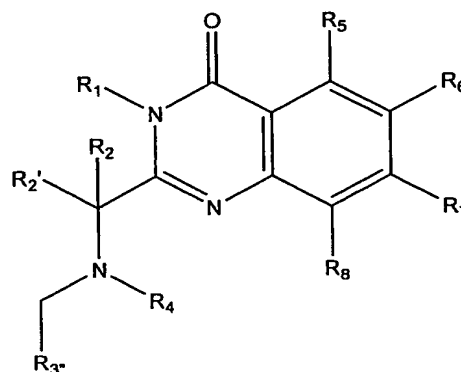
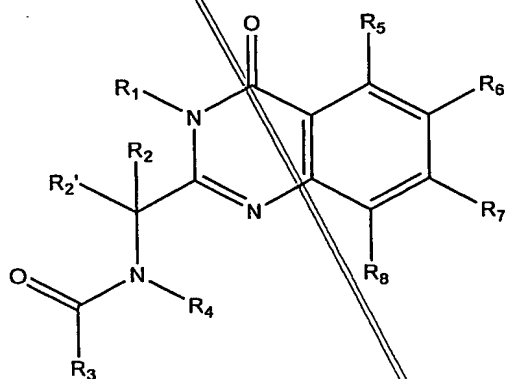
$R_{16}$  is di(lower alkyl)amino, (lower alkyl)amino, amino, lower alkoxy, or N-



formula as defined in Figure 3.

58. A method of screening for KSP kinesin modulators comprising:

(a) combining a kinesin, a candidate bioactive agent and a compound chosen from the group consisting of:



and

wherein:

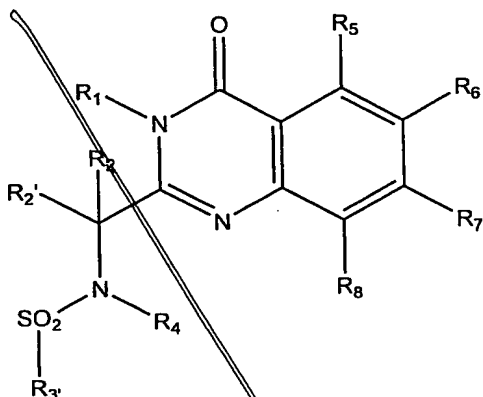
$R_1$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

$R_2$  and  $R_2'$  are independently chosen from hydrogen, alkyl, oxaalkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl; or  $R_2$  and  $R_2'$  taken together form a 3- to 7-membered ring;

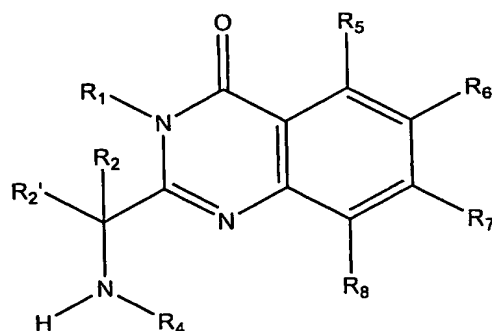
$R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, substituted alkylheteroaryl, oxaalkyl, oxaalkylaryl, substituted oxaalkylaryl,  $R_{15}O-$  and  $R_{15}NH-$ ;







and



wherein:

- $R_1$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl,  
 5 substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl,  
 and substituted alkylheteroaryl;  
 $R_2$  and  $R_2'$  are independently chosen from hydrogen, alkyl, oxaalkyl, aryl, alkylaryl,  
 heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted  
 alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl; or  $R_2$  and  $R_2'$   
 10 taken together form a 3- to 7-membered ring;  
 $R_3$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl,  
 substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl,  
 substituted alkylheteroaryl, oxaalkyl, oxaalkylaryl, substituted oxaalkylaryl,  
 $R_{15}O-$  and  $R_{15}NH-$ ;  
 15  $R_{3'}$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl,  
 substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl,  
 substituted alkylheteroaryl and  $R_{15}NH-$ ;  
 $R_{3''}$  is chosen from alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl,  
 substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted  
 20 alkylheteroaryl;  
 $R_4$  is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl,  
 substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl,  
 substituted alkylheteroaryl, and  $R_{16}$ -alkylene-;  
 $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are independently chosen from hydrogen, alkyl, alkoxy, halogen,  
 25 fluoroalkyl, nitro, dialkylamino, alkylsulfonyl, alkylsulfonamido,

sulfonamidoalkyl, sulfonamidoaryl, alkylthio, carboxyalkyl, carboxamido, aminocarbonyl, aryl and heteroaryl;

R<sub>15</sub> is chosen from hydrogen, alkyl, aryl, alkylaryl, heteroaryl, alkylheteroaryl, substituted alkyl, substituted aryl, substituted alkylaryl, substituted heteroaryl, and substituted alkylheteroaryl;

R<sub>16</sub> is chosen from alkoxy, amino, alkylamino, dialkylamino, N-heterocyclyl and substituted N-heterocyclyl; and

(b) determining the binding of said candidate bioactive agent to said kinesin.

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